DETAILED DESCRIPTION

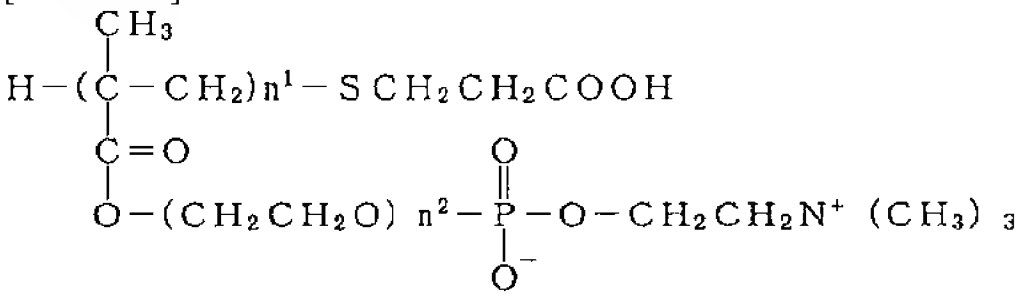
[Detailed Description of the Invention]
[0001]
[Field of the Invention]This invention relates to the dirt remover for contact lenses which makes an active principle ornamentation protein obtained by the manufacturing method and this manufacturing method of the ornamentation protein which combined with protein chemically the polymer containing a phosphorylcholine group.
[0002]
[Description of the Prior Art]As for the contact lens, the soft contact lens in which the main ingredients consist of polymer of the hard lens which consists of polymer of methyl methacrylate or silicon content methacrylate, and 2-hydroxyethyl methacrylate and methacrylic acid is used widely. However, in said hard lens. A silicon content group has high secrete (protein, lipid) and compatibility in tear fluid, since protein and lipid adhere to a contact lens easily, if it wears especially over a long period of time, it is polluted by lipid, protein, cosmetics, etc., cloudy weather occurs on a lens, and the fall of eyesight and the obstacle of an eye may be caused. The secrete in tear fluid adheres also in a soft contact lens, and also on the other hand, since water content is high, it is easy to produce contamination by the microorganism or bacteria, and cloudy weather occurs on a lens, and damage may be done to an eye.
[0003]Then, in order to remove the dirt of a contact lens conventionally, abrasive soap is further used for dirt according [a proteolytic enzyme] to lipid for the surface-active agent as a detergent by the dirt by protein at adherence dirt. However, although the detergent which consists of a surface-active agent and abrasive soap is effective to specific dirt, a detergency is insufficient or there is a problem that a lens may be damaged. On the other hand, the detergent which contains a proteolytic enzyme in JP,53-47810,B is proposed. However, since there is a life in the enzyme activity in solution, if it is neglected in the state of solution for 24 hours, the problem that enzyme activity falls arises and an improvement is desired.
[0004]In order to solve these problems, to JP,6-9504,A. The cleaning method from which the detergent which blended serine protease, an anionic detergent, etc. into glycerol rubs and washes a contact lens to JP,5-33768,B using the detergent which made the polyethylene glycol distribute a proteolytic enzyme is indicated. However, the problem that enzyme activity falls produces the detergent indicated to these by mixing with a dilution water.
[0005]By the way, in JP,6-313009,A, although the synthesizing method of end functionality phosphorylcholine group content polymer is indicated, about the ornamentation protein which made protein embellish these polymer chemically, and its use, it is not known conventionally.
[0006]
[Problem(s) to be Solved by the Invention]Even if it carries out long term storage of the purpose of this invention in the state of solution, there is in maintaining enzyme activity highly and providing the manufacturing method of the ornamentation protein which can be saved stably.
[0007]Other purposes of this invention are to provide the dirt remover for contact lenses excellent in preservation stability, without becoming dirty, even if the dirt removal ability of a contact lens is high and moreover carries out long term storage by solution states, and removal ability falling.
[0008]
[Means for Solving the Problem]According to this invention, it is a general formula (1).

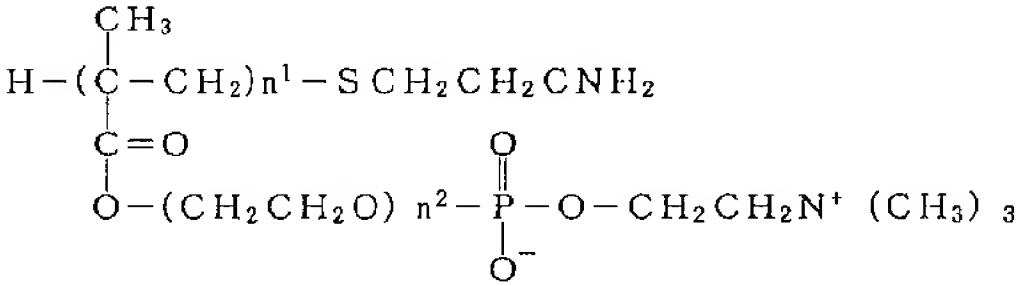
Pro-(R-(X^1) a-X) b ... (1)
(Pro shows among a formula proteinic residue and divalent organic residue to which R is derived from a functional group in protein, and a combinable functional group, and divalent organic residue in which X^1 does not contain a phosphorylcholine group, and X show organic residue of a compound containing a phosphorylcholine group.) a is 0 or 1 and b shows one or more positive numbers. It is in charge of manufacturing ornamentation protein expressed, and is a general formula (2).
R^1-(X^1) a-X ... (2)
(R^1 shows a functional group in protein, and a combinable functional group among a formula, and divalent organic residue in which X^1 does not contain a phosphorylcholine group, and X show organic residue of a compound containing a phosphorylcholine group.) a shows 0 or 1. A manufacturing method of ornamentation protein making a phosphorylcholine group content compound expressed and protein react is provided. Organic residue of a compound which contains a phosphorylcholine group shown by X in said general formula (2) according to this invention, It is the organic residue of 2-methacryloiloxy-ethyl phosphorylcholine, and a dirt remover for contact lenses, wherein protein contains ornamentation protein obtained by said manufacturing method which is hydrolase as an active principle is provided.
[0009]
[Embodiment of the Invention]In the manufacturing method of the ornamentation protein of this invention, the phosphorylcholine group content compound expressed with said general formula (2) and protein are made to react, and the organic residue of a compound which has a phosphorylcholine group obtains the ornamentation protein expressed with said general formula (1) chemically combined with protein.
[0010]In the phosphorylcholine group content compound expressed with a formula (2), R^1 is organic residue which has a functional group in protein, and a combinable functional group, and R in a formula (1) shows the divalent organic residue derived from the organic residue of R^1. As the functional group in this protein, and a combinable functional group, A hydroxyl group, a carboxyl group, an aldehyde group, an amino group, a sulfhydryl group, A SUKUSHINIMIJIRU oxycarbonyl group, an imide ester group, a halogeno nitro allyl group, A pyridino disulfide group, a maleimide group, a phthalimide thio group, a halogenomethylcarbonyl group, a halogeno carbonyl group, a halogeno sulfonyl group, a nitroazide phenyl group, an diazo trifluoroacetyl group, an isocyanate group, etc. are mentioned. In these, a carboxyl group and a SUKUSHINIMIJIRU oxycarbonyl group with an especially easy combination with the amino group in an enzyme, an isocyanate group, etc. are preferred among protein. As R in a formula (1), an amide group, JIKARUBAMIDO combination, urea combination, a disulfide bond, an imidic acid amide bond, 3-thiosuccinimide group (combination in which the thiol group was formed in response to the maleimide group), etc. can be mentioned preferably.
[0011]It is not what X^1 is divalent organic residue which does not contain a phosphorylcholine group in a formula (1) and (2), and is limited especially, A thioester group, an ether group, an alkylene group, an oxyalkylene group, a polyoxyalkylene group, an alkylene urethane group, a sulfonyl group, etc. are mentioned. The organic residue of the compound which, on the other hand, contains the phosphorylcholine group expressed with X will not be limited especially if it is the residue which contains organic residue at the end.
[0012]As a phosphorylcholine group content compound expressed with a formula (2), the polymer etc. which are shown with a following formula can be mentioned preferably. However, as for n^1, the positive

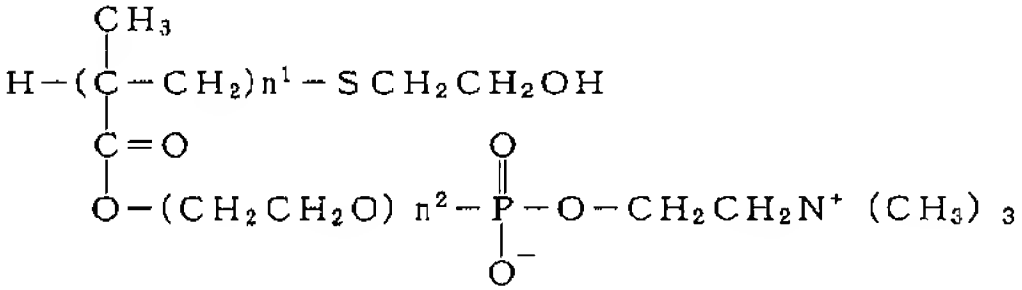
number of 1-10000 and n^2 show the positive number of 1-10000, as for the positive number of 1-1000, and n^3. Manufacture is difficult when n^1 and n^3 exceed 10000, and n^2 exceeds 1000.

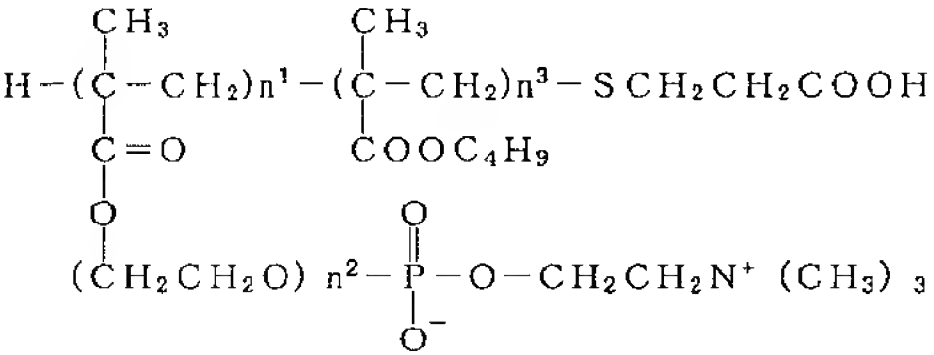
[0013]

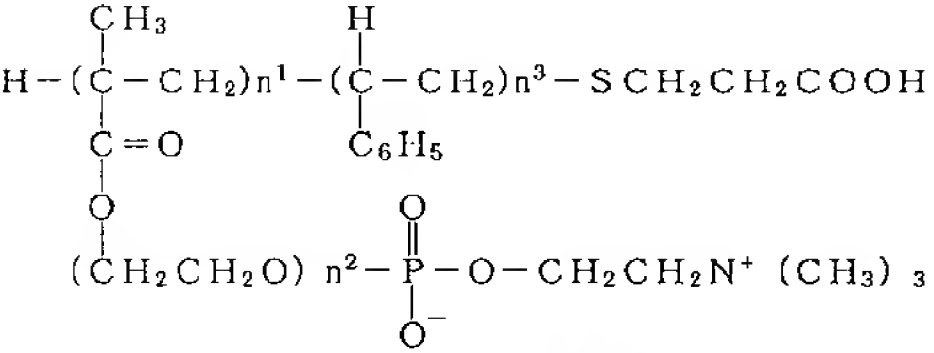
[Formula 1]

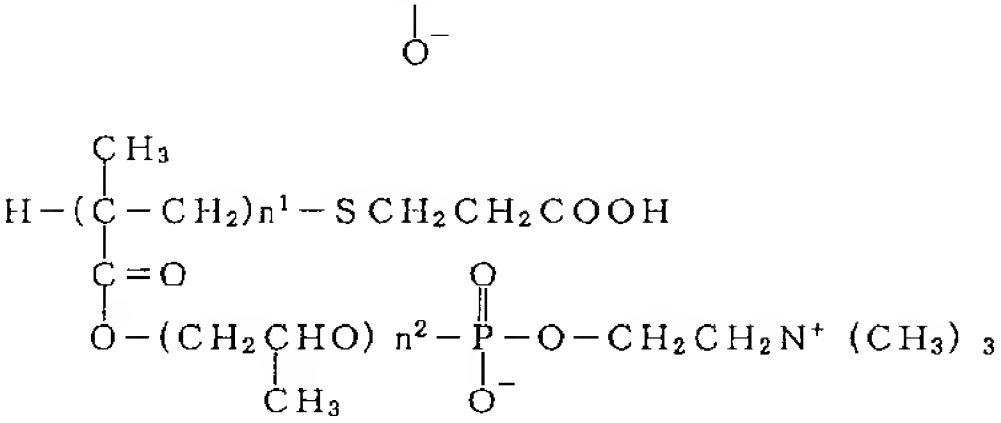












[0014]Although the molecular weight in particular of the phosphorylcholine group content compound expressed with a formula (2) is not limited, In order not to reduce preferably the activity (enzyme activity etc.) of the number average daily doses 500-1 million and the protein mentioned especially later preferably, the range of the number average molecular weights 1000-100000 is preferred.

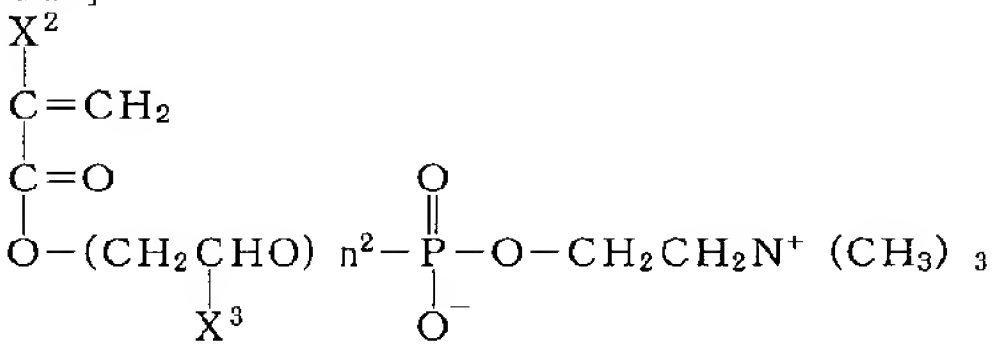
[0015]Although a method in particular of compounding a phosphorylcholine group content compound expressed with a formula (2) is not limited, A monomer which contains a phosphorylcholine group under existence of a specific radical chain transfer agent which constitutes R^1 in a formula (2) by known polymerization art, such as solution polymerization or mass polymerization, for example, other independent or copolymerizable vinyl monomers, It can obtain by a method of polymerizing using a radical polymerization initiator, etc.

[0016]Although not limited especially as a radical chain transfer agent which constitutes R^1 in a formula (2), and also R of a formula (1), thioglycolic acid, a thioglycol, an aminoethane thiol, ethanedithiol, etc. are mentioned.

[0017]as a monomer containing a phosphorylcholine group which constitutes X (X in a formula (1)) in a formula (2), phosphorylcholine group content (meta-) acrylate etc. which are shown with a following formula (3) can be mentioned.

[0018]

[Formula 2]



(式中、X^2及びX^3は、同一又は異なる基であって、水素原子又は

メチル基を示す。またn^2は１～１０００の整数を示す。)

[0019]As said phosphorylcholine group content (meta) acrylate, 2-(meta) acryloyloxyethyl phosphorylcholine, 2-(meth)acryloyloxy 1-methylethyl phosphorylcholine, 2-(meta) acryloyloxypropyl

phosphorylcholine, 2-(meth)acryloyloxy ethoxyethyl phosphorylcholine, beta -(2'-(meth)acryloyloxy 1'-methylethoxy)- Propyl phosphorylcholine, 2-(meta) acryloyl oxydi ethoxyethyl phosphorylcholine, etc. can be mentioned.

[0020]As a monomer containing said phosphorylcholine group which constitutes X^1 (X^1 in a formula (1)) in a formula (2), and a copolymerizable vinyl monomer, For example (meta), acrylic acid-n-butyl, methyl acrylate (meta), (Meta) Ethyl acrylate, butyl acrylate (meta), acrylic acid (meta) pentyl, (Meta) Acrylic acid hexyl, acrylic acid (meta) heptyl, acrylic acid (meta) octyl, (Meta) Tridecyl acrylate, acrylic acid (meta)-2-ethoxyethyl, (Meta) Acrylic acid, acrylic acid (meta)-2-hydroxyethyl, (Meta) Acrylic acid amide, acrylic acid (meta)-N,N'-dimethylamide, Vinyl acetate, N-vinyl pyrrolidone, styrene, alpha-methylstyrene, Methylene nuclear substitution styrene, chloro nuclear substitution styrene, VCM/PVC, a vinylidene chloride, Ethylene, propylene, isobutylene, vinyl propionate, ethyl vinyl ether, n-butylvinyl ether JIERIRU itaconate, di-n-butyl itaconate, etc. can be mentioned, and especially methacrylic acid ester etc. are preferred. When using it, it can be independent or can use as a mixture.

[0021]As said radical polymerization initiator, 2,2'-azobisisobutyronitrile, azobisma leno nitril, benzoyl peroxide, lauroyl peroxide, diisopropylperoxy carbonate, ammonium persulfate, potassium persulfate, etc. can be mentioned, for example.

[0022]Although a non-solvent can also perform a polymerization reaction which compounds a phosphorylcholine group content compound shown by a formula (2), it is preferred to use a solvent, in order to perform a polymerization reaction more smoothly. What is meltable in a monomer as this solvent, for example, water, methanol, Ethanol, propanol, butanol, acetone, methyl ethyl ketone, a tetrahydrofuran, dioxane, dimethylformamide, acetonitrile, chloroform, a methylene chloride, benzene, ethyl acetate, or these mixtures can be mentioned.

[0023]As for monomer concentration at the time of compounding a phosphorylcholine group content compound expressed with a formula (2), l. is especially desirable in 0.2-1.0 mol /0.1-10 mol/l. so that it may become said molecular weight preferably. As for concentration ([S] /[M]) to a monomer of a chain transfer agent, 0.005-2, especially 0.01-1 are desirable to said monomer concentration. As for the ratio of concentration ([S]/[I]) to a radical polymerization initiator of a chain transfer agent, it is desirable 1.0-500, and for chain transfer agent concentration to add to this radical polymerization start agent concentration, so that it may become especially the range of 1.0-200.

[0024]As for especially polymerization temperature at the time of compounding a phosphorylcholine group content compound expressed with a formula (2), 30-90 ** is desirable 20-100 **. Polymerization time is about 1 to 72 hours. When carrying out copolymerization of said 2-methacryloiloxy-ethyl phosphorylcholine and other copolymerizable vinyl monomers, said vinyl monomer has preferred 0-95-mol% of range to the monomer whole quantity, and is desirable. [0-50 mol% to which especially enzyme activity is not reduced of]

[0025]Protein used in a manufacturing method of this invention constitutes a basis expressed with Pro in a general formula (1), and as protein, For example, an antibody to peptide, an enzyme, various antigens, or an antigen which has reactive functional groups, such as a hydroxyl group, a carboxyl group, an amino group, and an aldehyde group to which ring breakage of the various sugar chains was carried out, and has biological catalysis, etc. can be mentioned. As an enzyme, hydrolase, redox enzyme, transfer enzyme, lyase, isomerase, synthetic enzyme, etc. can be mentioned. As hydrolase, peptidase; lipase, such as protease, Ester hydrolysis enzymes, such as phospholipase and alkaline phosphatase; sugar hydrolysis enzymes, such as beta-D-galactosidase, amylase, cellulase, hemicellulase, saccharase, and a

pectinase, etc. are mentioned. A commercial item can also be used, for example, a trade name "BIOPURAZE" (the Nagase Brothers Seikagaku make, peptidase), a trade name "lipase SAIKEN" (the Nagase Brothers Seikagaku make, ester hydrolysis enzyme), etc. are mentioned. Under the present circumstances, the origin of an enzyme is not limited but can use a thing of all the origins, such as a bacillus (Bacillusu).

[0026]As an antigen or an antibody, for example C reactive protein (CRP), a rheumatism factor (RF), Plasma proteins, such as transformer Felice, and an antibody to these; Thyrotropic hormone (TSH), T three (T_3), thyroxine (T_4), thyroxine binding nature protein (TBG), Thyroglobulin, an insulin, estriol (E_3), chorionic gonadotropin (HCG), An antibody to hormone, such as human placenta nature lactogen (HPL); A carcinoembryonic antigen (CEA), Tumor related substances, such as beta$_2$-micro globulin and alpha fetoprotein (AFP), and an antibody to these; An HBs antigen, An antigen to an antibody to an antigen or antibodies of a hepatic fever, such as a HBs antibody, an HBe antigen, and a HBe antibody; Mumps, An antibody or antigens to various biogenic substances, such as herpes, measles, German measles, a virus of site megalo-**, and an anti-acquired immunodeficiency syndrome antibody (HIV); an antibody to various drugs, such as phenobarbital, acetamino phenon, salicylic acid, and cyclosporin, is mentioned.

[0027]In order to make a phosphorylcholine group content compound and protein which are expressed with a formula (2) react in a manufacturing method of this invention, For example, a phosphate buffer solution, carbonic acid buffer solution, acetic acid buffer solution, tris / chloride buffer solution, In a solution which dissolved an enzyme in various physiological salines etc., or dimethylformamide, A solution which dissolved a phosphorylcholine group content compound as an ornamentation agent in a tetrahydrofuran, water, methanol, ethanol, propanol, or these mixed liquor can be added, and reaction temperature of 0-50 ** can carry out by a method of making it react for - 24 hours during reaction-time 15 minutes, etc. Ornamentation protein which is a resultant can be used, without generating, and can also be refined by methods, such as dialysis, curing salting, and gel filtration, as occasion demands.

[0028]As a concrete reaction, when R^1 of a formula (2) is a carboxyl group or a hydroxyl group, for example, In a solution made dissolved or suspended, a phosphorylcholine group content compound as an ornamentation agent. 1,1'-carbonyl bis-1H-imidazole, a 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide, By adding in a solution in which protein was dissolved directly, after adding condensing agents, such as dicyclohexylcarbodiimide, and making them react, Or after adding said condensing agent, adding N-hydroxysuccinimide etc. further and making it react, ornamentation protein expressed with a general formula (1) can be obtained by adding in a solution in which protein was dissolved. When R^1 of a formula (2) is an amino group, for example, After making a glutaraldehyde solution etc. add and react to a solution which made a phosphorylcholine group content compound as an ornamentation agent dissolved or suspended, ornamentation protein expressed with a general formula (1) is obtained by adding in a solution in which protein was dissolved. R^1 of a formula (2), for example A SUKUSHINIMIJIRU oxy cull BONITSU group, In the case of active ester groups, such as an imide ester group, a halogeno nitro allyl group, a pyridino disulfide group, a maleimide group, and a phthalimide thio group, Ornamentation protein expressed with a general formula (1) can be obtained by adding a phosphorylcholine group content compound as an ornamentation agent which has an active ester group the dissolution or directly in a solution in which protein was dissolved.

[0029]Organic residue of a compound which has a phosphorylcholine group expressed with a general

formula (1) can combine chemically with protein ornamentation protein obtained by a manufacturing method of this invention, and Pro in a formula, R, X^1, and X can mention the above-mentioned thing preferably. b in a formula (1) -- one or more positive numbers -- although preferably based also on a proteinic kind -- 1-100 -- it is 1-10 still more preferably. If b exceeds 100, it will be based also on a proteinic kind, but since proteinic activity (enzyme activity, antibody activity, etc.) may fall, it is not desirable. The number of b of compound ornamentation protein can be determined by quantifying a functional group in compound ornamentation protein. For example, when this functional group is an amino group, an amino group in protein before a reaction and after a reaction can be quantified, an embellished amino group can ask for it comparatively (ornamentation rate), and the number of b can be determined from this ornamentation rate.

[0030]A dirt remover for contact lenses of this invention contains ornamentation protein produced by X in said general formula (2) making a phosphorylcholine group content compound shown by a formula (2) which is the organic residue of 2-methacryloiloxy-ethyl phosphorylcholine, and hydrolase react as an active principle. Although effective concentration of this active principle changes with kinds and activity of hydrolase, when a dirt remover for contact lenses is made liquefied, it is usually the range of 0.1-100mg/ml preferably 0.01mg/ml or more.

[0031]The dirt remover for contact lenses of this invention can also blend an ingredient usually used as a dirt remover for contact lenses, or an ingredient of a penetrant remover in addition to said active principle. Specifically, a surface-active agent, an isotonizing agent, an antiseptic, a chelating agent, a pH adjuster, etc. are mentioned. As a surface-active agent, any surface-active agent of cationicity, anionic, nonionicity, or both sexes can be used. A desirable surface-active agent nonionicity or neutral is desirable. [, such as polyethylene glycol ester, polyethylene glycol ether, a polypropylene glycol, and a polyethylene glycol,] As an isotonizing agent, mineral salt, such as sodium chloride and potassium chloride, etc. are mentioned. As a chelating agent, ethylenediaminetetraacetic acid (EDTA) or its alkali metal salt, citrate, tartaric acid, etc. are mentioned.

[0032]A gestalt of a dirt remover for contact lenses of this invention is liquefied, and also may be dryness, such as powder and a tablet. In the case of such dryness, it can also be used for a medium suitable at the time of use, dissolving. On the other hand, since an active principle is the hydrolase chemically embellished with a polymer containing 2-methacryloiloxy-ethyl phosphorylcholine when liquefied, even if it is liquefied for a long period of time and being saved, enzyme activity can be maintained highly and, for this reason, dirt removal ability (washing ability) hardly falls.

[0033]In order to remove dirt of a contact lens using a dirt remover of this invention, What is necessary is to dip a contact lens in this diluent and just to settle for 15 to 120 minutes, after dipping a contact lens in a dirt remover of solution states or diluting a dirt remover of solution states or dryness with buffer solution, an isotonic solution, or conservation liquid for contact lenses. Under the present circumstances, it may heat. Although grinding washing may be carried out, even if it does not carry out grinding washing in many cases, decomposition removal of the dirt can be efficiently carried out by operation of hydrolase. After removing dirt, it can rinse and equip with a contact lens with a suitable rinse.

[0034]

[Effect of the Invention]In the manufacturing method of the ornamentation protein of this invention, even if it carries out long term storage by solution states, the protein to which chemical modification of the protein activity (enzyme activity etc.) was carried out with the phosphorylcholine group content compound which hardly falls can be obtained. Since the specific repair enzyme obtained by said

manufacturing method is contained as an active principle, the dirt remover for contact lenses of this invention can be saved without being able to maintain enzyme activity highly and reducing most dirt removal ability (washing ability) for this reason, even if it is liquefied for a long period of time and being saved.

[0035]

[Example]Hereafter, although a reference example, an example, and a comparative example explain still in detail, this invention is not limited to these.

[0036]The preparation ethanol of 2-methacryloiloxy-ethyl phosphorylcholine polymer (polymer a) which has carboxylic acid at the one to reference example 1 end is used as a solvent, 0.45 mol/l. 2-methacryloiloxy-ethyl phosphorylcholine solution is prepared, it becomes $9x10^{-4}$mol / liter about azobis isobutylnitril as the quantity which becomes this solution in l. and 0.09 mol /about 3-Merca prop Ropion acid as a chain transfer agent, and a radical polymerization initiator -- quantity mixing was carried out. 60 ** of obtained solutions were polymerized after freezing deaeration and the vacuum sealed tube by the sealed tube method for 6 hours. After being dropped after ending reaction and into ether and collecting precipitation, the polymer a which washes, carries out reduced pressure drying and has carboxylic acid at the end of the number average molecular weight 20000 was prepared.

[0037]The preparation ethanol of 2-methacryloiloxy-ethyl phosphorylcholine / n-butyl methacrylate copolymer (polymer b) which has carboxylic acid at the one to reference example 2 end is used as a solvent, 2-methacryloiloxy-ethyl phosphorylcholine concentration prepares the solution in which 0.40 mol [l.] /and n-butyl methacrylate concentration become in l. and 0.05 mol /, The quantity which becomes this solution in l. and 0.09 mol /about 3-Merca prop Ropion acid as a chain transfer agent, The solution which serves as $9x10^{-4}$mol / liter in azobis isobutylnitril as a radical polymerization initiator and which was obtained by carrying out quantity mixing was made to react like the reference example 1-1, and the polymer b of the number average molecular weight 55000 was prepared.

[0038]It was made to dissolve in 6.5 ml of 0.01M phosphate buffer solutions (pH 7.6), and polymer a 580mg and 54.8 mg (0.002mmol) of trade names "BIOPURAZE" (the Nagase Brothers Seikagaku make, molecular weight 27000 [about]) which were prepared by the one to example 1 reference example 1-1 were made to ice-cool. Then, 153.4 ml of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimides were added, and it agitated for 1 hour. After adding 153.4 mg (0.80mmol) of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochlorides again and agitating for 1 hour, it agitated at the room temperature for further 1 hour. After ending reaction, Permeable membrane (spectrum Medical Industries Inc., trade name "Spectrum/por, membranes MW CO. 6000-8000) performs dialysis of as opposed to 0.01M phosphate buffer solution (pH 7.6) for reaction mixture, The unreacted 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide was removed. The obtained compound was ornamentation BIOPURAZE shown with a following formula (4).

$E\text{-}(NH\text{-}CO\text{-}(CH_3)\ S\text{-}P^1)\ n$ ... (4)

(E shows the residue of a trade name "BIOPURAZE" among a formula, and P^1 shows the end residue of the polymer a.) n is 4.7. A reference solution and the ornamentation rate of an unembellished trade name "BIOPURAZE" are made [the rate (ornamentation rate (%)) in which the isolation amino group in a trade name "BIOPURAZE" carried out the amide bond to the carboxyl group of the polymer a] into 0% for a glycin solution, It measured based on the assay (Analytical Biochemistry 14,328-336 (1966)) of an isolation amino group. As a result, the ornamentation rate was 52.8% and n was 4.7.

[0039]Ornamentation BIOPURAZE which carries out like Example 1-1 and is expressed with a following formula (5) was obtained except having used the polymer b prepared by the reference example 1-2 instead of the polymer a prepared by the reference example 1-1 used in one to example 2 Example 1-1.

E-(NH-CO-(CH_3) S-P^2) n ... (5)

(E shows the residue of a trade name "BIOPURAZE" and P^2 shows the end residue of the polymer b.) n is 4.5. Like Example 1-1, the isolation amino group in a trade name "BIOPURAZE" made [the rate (ornamentation rate (%)) which carried out the amide bond to the carboxyl group of the polymer b] 0% the reference solution and the ornamentation rate of the unembellished trade name "BIOPURAZE" for the glycin solution, and measured the ornamentation rate like Example 1-1. As a result, the ornamentation rate was 49.5% and n was 4.5.

[0040]3.00 g (1.0mmol) of comparative example 1-1 monomethoxy polyethylene glycols (CH_3O (CH_2CH_2O) nCH_2CH_2COOH) (number average molecular weight 3000) were dissolved in 50.0 ml of 1,4-dioxane. Subsequently, 138.12 mg (1.2mmol) of N-imide hydroxysuccinate and 247.60 mg (1.2mmol) of dicyclohexylcarbodiimide were added, and it was made to react at a room temperature for 6 hours. After ending reaction, reaction mixture was dropped at 500 ml of hexane, and the polyoxyalkylene derivative was settled. After filtering settlings and making it fully wash by hexane, reduced pressure drying was carried out and 2.67 g (0.89mmol) of polyoxyalkylene derivatives (the polymer c is called below) of white powder were obtained.

[0041]It was made to dissolve in 6.5 ml of 0.01M phosphate buffer solutions (pH 7.6), and 54.8 mg of trade names "BIOPURAZE" (the Nagase Brothers Seikagaku make, molecular weight 27000 [about]) were made to ice-cool. Then, after adding said polymer c60.89mg and agitating for 1 hour, it agitated at the room temperature for further 1 hour. Dialysis of as opposed to 0.01M phosphate buffer solution (pH 7.6) for reaction mixture was performed like Example 1 after ending reaction, and ornamentation BIOPURAZE expressed with a following formula (6) was obtained.

E-(NH-CO-CH_2CH_2(CH_2CH_2O) nOCH_3) n ... (6)

(E shows the residue of a trade name "BIOPURAZE" among a formula.) n is 5.5. The reference solution and the ornamentation rate of the unembellished trade name "BIOPURAZE" were made [the rate (ornamentation rate (%)) in which the isolation amino group in a trade name "BIOPURAZE" carried out the amide bond to the succinimide group of the polymer c] into 0% for the glycin solution, and it asked for the ornamentation rate like Example 1-1. As a result, the ornamentation rate was 52.8%, and n was 4.7.

[0042]The repair enzyme prepared in two to example 1 Example 1-1 was dissolved in the physiological saline so that it might become 0.4% of the weight of concentration, and the dirt removing liquid for contact lenses was prepared. It washed in the state where this dirt removing liquid was made to immerse and settle the contact lens to which protein was made to adhere. The cleaning effect was performed visually 2 hours afterward, and the case where adhesion protein was almost removed was judged as poor in fitness and except [its]. A result is shown in Table 1. The contact lens to which protein was made to adhere was prepared as follows. Namely, artificial tear fluid (the albumin 0.6g, 0.3 g of globulin, and 0.2 g of lysozymes) The contact lens (the SEIKO contact lens company make, trade name "super EX1") was dipped in what was made to dissolve 0.1 g of mucin in a physiological saline, and was 100 ml, it heated

at 65 **, and protein was made to adhere.
[0043]The enzyme activity of the proteolytic enzyme of this dirt removing liquid was measured according to the casein Folin method immediately after dirt removing liquid preparation and 14 weeks afterward (it saves at 40 **). A result is shown in Table 1.
[0044]Except having used the repair enzyme prepared in Example 1-2 instead of the repair enzyme prepared in two to example 2 Example 1-1, it became dirty like Example 2-1, removing liquid was prepared, and each measurement was performed. A result is shown in Table 1.
[0045]Except having used the unembellished trade name "BIOPURAZE" (the Nagase Brothers Seikagaku make, molecular weight 27000 [about]), it became dirty instead of the repair enzyme prepared in two to comparative example 1 Example 1-1 like Example 2-1, removing liquid was prepared to it, and each measurement was performed to it. A result is shown in Table 1.
[0046]Except having used the repair enzyme prepared by the comparative example 1-1 instead of the repair enzyme prepared in two to comparative example 2 Example 1-1, it became dirty like Example 2-1, removing liquid was prepared, and each measurement was performed. A result is shown in Table 1.
[0047]
[Table 1]

	蛋白質分解酵素の酵素活性(%)	洗浄効果
実施例2-1	１００	良好
実施例2-2	９９	良好
比較例2-1	検出できず	不良
比較例2-2	７５	不良

[0048]Even if the repair enzyme which combined with the enzyme chemically the polymer containing 2-methacryloiloxy-ethyl phosphorylcholine has a good cleaning effect and it moreover carries out long term storage in the state of solution from the result of Table 1, it hardly falls but, as for enzyme activity, it turns out that it is maintained highly.

[Translation done.]